Non-invasive Ventilation (NIV): Are we throwing some babies out with the bathwater?

Rob Graham, R.R.T./N.R.C.P..

I dedicate this and future columns to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

Since before I watched Dr. Jackie Coalson present her baboon model of non-invasive continuous positive airway pressure (CPAP) vs. invasive ventilation at the 21st Snowbird conference in 2004, (1) I was convinced early extubation, use of non-invasive ventilation (NIV) and avoidance of invasive ventilation where appropriate was the future. Years later most of us are riding happily along on the NIV bus on the road we assume leads to better outcomes. Speeding along, however, no one seems to have checked the brakes. Who are these "appropriate" babies? And how do we decide when NIV is leading us in the wrong direction?

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Since the journey began, things have changed. The COIN trial (2) examined infants stratified at 25-26 weeks and 27-28 weeks. It did not show any benefit to NIV and showed more air leak in the CPAP group. Examining the management, to me, could be a clue as to why. The CPAP level used was 8 cmH_20. "PEEPaphobia" (3) it seems persists in the absence of an endotracheal tube (ETT). To quote Dr. Bert Bunnell, "meaningful, sustained recruitment will not occur below a mean airway pressure (MAP) of 10 cmH_20". In my experience and practice, I concur. I soon discovered on the admission table using the first HFO capable machine I'd ever had that a frequency of 10, MAP of 10 cmH_2O, and 100% amplitude (it was a weak machine) worked most of the time. The increased risk of an air leak in the trial's CPAP group to me indicates air trapping, which can occur with CPAP if adequate pressures are not reliably maintained. Whatever pathological label one gives it, these babies' lungs can get quite crappy, and quite quickly at that. Figure 1 is a chest film is of an infant on CPAP, never intubated. There are signs of de-recruitment despite "good volume" by rib count. Figure 2 is the same baby. This is not a post-extubation film. This baby has never been intubated at this point. This is not what we expected when we boarded the NIV bus. Figure 3 is the post-intubation chest film, the first with an ETT in situ.

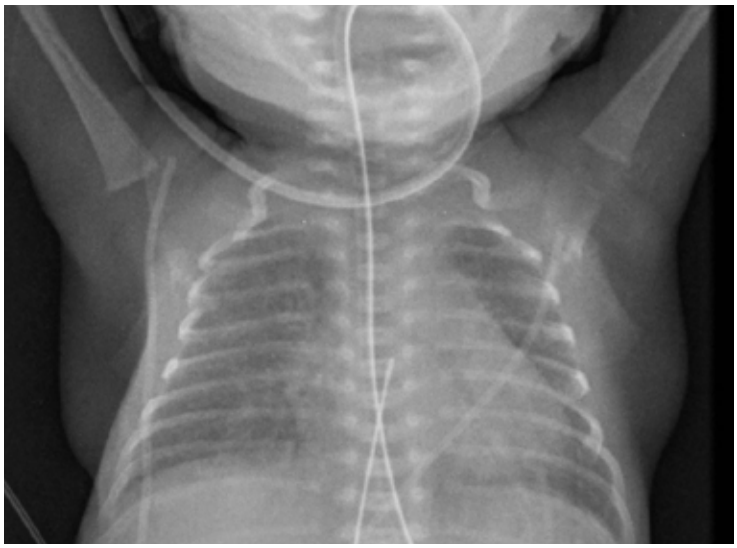

Figure 1

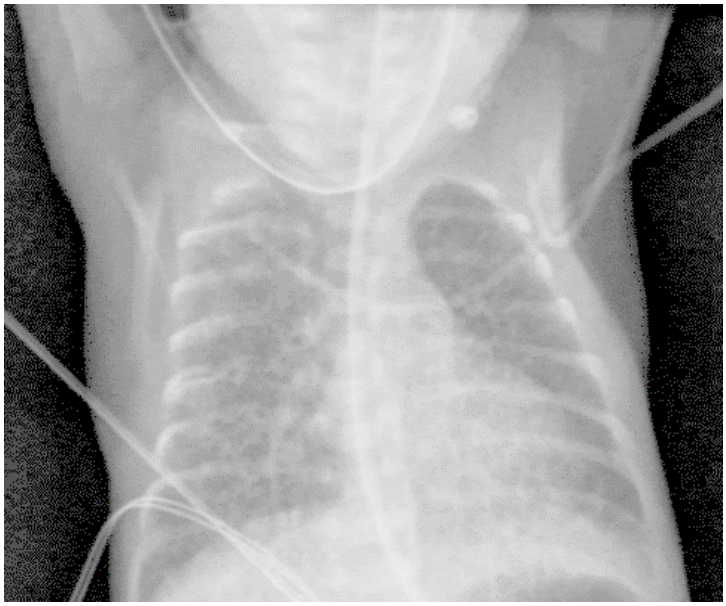

Figure 2

As with any therapy, it is best to choose patients wisely. Many centres are now approaching the resuscitation of sub-23-week gestation infants the way sub-25 week infants were 20 years ago, and many are keen to prevent chronic lung disease (CLD) by avoiding an ETT. As my mother would say, "you can't make a silk purse from a sow's ear." From a physiological perspective, it is unrea-

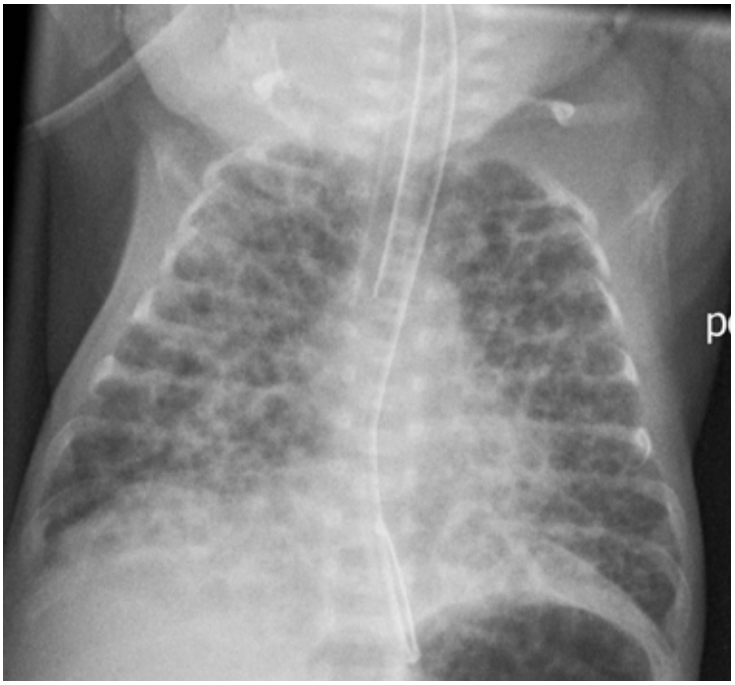

Figure 3

sonable to expect a structure that is not yet a lung to be a fully functioning lung, nor an immature respiratory centre to maintain spontaneous breathing. My own experience suggests only 5-10% of sub-25-week infants will avoid an ETT. Hence the necessity of knowing how to ventilate is still de rigueur.

Why, even though approached with gusto, the best of intentions and the appropriate patient, is NIV failing some? Those enamored with conspiracy theories will surely love this tale, for indeed conspiracy and double-crosses abound. The nature of the patient, limitations of equipment, and sometimes misguided practices share the blame.

The Patient

Many of the same challenges facing clinicians when mechanically ventilating are present without an endotracheal tube. The primitive lung is lacking in both structure and function. Decreased surface area for gas exchange may require higher minute volumes for ventilation and oxygenation, and lack of vasculature compounds the problem. It can be difficult to oxygenate without hyperventilating since CO_2 diffuses twenty times more readily than O_2. Babies may hyperventilate on CPAP when they do not achieve proper functional residual capacity (FRC) just as when genuinely hyperinflated. Floppy airways collapse easily and require substantial CPAP levels to maintain patency. Failure to do so will result in air trapping downstream, and airways are still small with accompanying high flow resistance. While the ETT may be absent, the gastric tube (GT) is quite present. Required for venting and feeding, the GT may also help gas enter the stomach when pressures are high; more gas in the stomach and abdomen leave less room for gas in the lungs, requiring ever higher pressures contributing to feeding intolerance and perhaps aspiration. And then there's that respiratory centre… always asleep at the switch! While non-invasive positive pressure ventilation (NIPPV) may help, the evidence is lacking to support this mode unless accompanied by diaphragmatic triggering. I was using NIPPV via a nasopharyngeal tube in the late '80s. Babies graduated to CPAP when someone forgot to turn the machine back on after an NPT change, and the baby didn't notice.

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I think there is a case to be made to have micro-prems intubated and ventilated lung protectively to reduce the risk of cerebral hemorrhage: stimulation to breathe is startling, a response we do not want to elicit in the first 72 hours of a micro-prem's life. Finally, there is oxygen. To quote Dr. Martin Keszler, "CPAP with high FiO_2 indicates atelectasis and may be worse than intubation, surfactant administration, and lung protective ventilation". (4) The micro prem has little to no endogenous antioxidant protection and is very prone to oxidative stress and injury. Recent studies out of the U.K. allude to increased, sustained oxygen levels leading to poorer one second forced expiratory volumes in children managed with NIV as babies and another out of Australia suggests the overall incidence of CLD is not falling despite the use of NIV. (5) Last but not least, the extreme susceptibility to intraventricular hemorrhage let alone pain leave a clinician ill-advised to intubate without proper anesthesia unless an infant is flat. This requires time. Should apnea be the only problem and FiO_2 is low, this is not a problem. If FiO_2 is high, however, the clock is ticking, but instead of a bomb going off all at once, the damage starts immediately and grows exponentially. We see the inflammatory response about a week later. In the old days, that's when babies who were in room air (and by my current standards over ventilated and with an archaic mode) suddenly jumped up in oxygen requirements.

The chest films were BPD or the start of it.

The Equipment

A challenge to the successful delivery of NIV is MAP; the maintenance of sufficient MAP at pressures above 12 cmH20 with current equipment is, I think, a challenge everywhere, and if using the Viasys®Sipap® impossible due to the pressure blow off on the machines. A large amount of dead space, the absence of synchronization with NIPPV, and difficulty measuring tracheal pressure in NIV all collude to lessen the chance of success in the micro prem. Leaks, whether around the interface or through the mouth, dead space, and the dreaded skin breakdown and pressure sores are all very real problems we face today when higher MAP is required. I use non-invasive high-frequency oscillation (NIHVO) in my practice frequently. While there are no clinical trials to support this mode (and it is not at this time available in the U.S.), it seems to work quite well on little babies and is less affected by leaks than NIPPV. As for gastric distention, I cannot say it is better or worse, but minimising amplitude may help. CPAP is, I think, the best tolerated of NIV modes in the absence of persistent apnea.

The Clinician

Any mode of ventilation will fail if the clinician will not provide the pressure required to achieve and maintain adequate FRC. This is as true with NIV as with any invasive mode. There seems to be a great reluctance to use "high" CPAP pressures during resuscitation. One should not be afraid to use pressures of 10-15 cmH_2O or more during initial recruitment. It's not about the size of the baby; it's about the stiffness of their lungs. Once airways are open pressure can be decreased to 10 or less providing there is not a rebound in O_2 requirements. A baby gasping and grunting to try and achieve FRC is quite capable of blowing a spontaneous pneumothorax, and that happens when one doesn't provide enough support. Another common clinical approach is the acceptance of high FiO2 levels, sometimes greater than 0.60. An adult cannot live indefinitely in 70% O_2, what makes anyone think a 25 weeks gestation infant can? I think this may be well intentioned, but it is wrong. The old idea that 40% O_2 is okay comes from back in the days when a 29 weeks infant was considered a micro prem and surfactant was a dream. Most patients then were above 30 weeks and far less prone to oxygen toxicity than the extremely prema-

ture infants we treat today. With the only crude, conventional and non-synchronised ventilators to use and no surfactant, 40% O_2 wasn't okay either, but it was necessary. NIV CPAP/MAP should be titrated as tolerated to the lowest possible FiO_2 requirements, for it is there that one has achieved the best balance between ventilation, perfusion, and compliance. Finally, I think that failure must be recognized when it happens, and failure criteria that reflect the needs of the baby and not the wishes of the clinician should be well established when using NIV. Quoting Dr. Keszler again, "If CPAP level is not sufficient to achieve the "open lung," the lung is subject to volutrauma and atelectotrauma just like with mechanical ventilation". (4) I concur. Once this happens, an inflammatory cascade ensues. The lung is most prone to damage when being recruited, and since de-recruitment is rarely homogeneous, the lung is even more prone to damage during recruitment at this point than during resuscitation.

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Hope for the Future

A study has been done using diaphragmatic monitoring (EDI) comparing CPAP with a conventional interface and the RAM® cannula to compare workload between the two. (6) I mention this only because of the use of EDI in NIV. I would like to see similar studies done on NIHFO and NI jet ventilation. Managing babies on the former routinely and having done the latter once (I'll tell you about it, I promise!) I am curious to see the utility of EDI in assessing proper PEEP/MAP settings both in NIV and invasive modes. If we can avoid X-rays and simply allow the baby to show us what they need in terms of MAP it would be a godsend clinically, and perhaps be the tool that improves the success of any mode of ventilation. Optimal compliance should be reflected as the least work on EDI. It is hoped the technology is made available through license eventually or a portable interface made for clinical monitoring applications. Those on a budget will balk at spending over $70k to provide non-invasive ventilation no matter what song the machine plays, but from an evidence-based standpoint, I think it a relative bargain if it can be shown to reduce costs later in life if not in the hospital. Proteomics hold promise in helping to find markers for those at risk of damage from not just a pulmonary, but whole system standpoint. And NIV research is really just beginning. When oscillation with volume control becomes available in the U.S., so will the research on HFO.

That mechanical ventilation comes at a cost is without question; there is, however, an ongoing need for it. It is possible to mechanically ventilate micro prems protectively. If a unit has high CLD rates amongst infants who are ventilated but who are good candidates for NIV stops ventilating these infants and, rather, adopts an NIV approach to management, CLD rates will indubitably drop. A unit having relative success mechanically ventilating smaller, less mature babies may not see such a dramatic decrease applying the same approach; they may even see them rise. Infants less than 25 weeks are very likely to require mechanical ventilation. Delayed recruitment and early oxidative stress may actually impair the outcome of these babies compared to immediate, appropriate mechanical ventilation and control of CO_2 levels for 72 hours for neuroprotection. My bias is towards HFO and HFJV; a bias gained through witness. In my practice I have seen CLD rates decline and remain low even though gestational age is decreasing. I know it can be done. NIV is, I think irrefutably, part of the solution, that is, as long as it does not get in the way of it.

References:

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3 *PEEPaphobia: an unreasonable or irrational fear of PEEP, generally greater than 6 or 7.*
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5 http://www.nicuethosandevidence.com/wp-content/uploads/2017/07/Doyle-et-al-2017-Ventilation-in-ELBW-and-Lung-Function-at-8-Years.pdf
6 https://doi.org/10.1038/s41372-019-0333-x

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Rob Graham, R.R.T./N.R.C.P.
Advanced Practice Neonatal RRT Sunnybrook Health Science Centre
43 Wellesley St. East
Toronto, ON
Canada M4Y 1H1
416-967-8500
Rob Graham <rcgnrcp57@yahoo.ca>